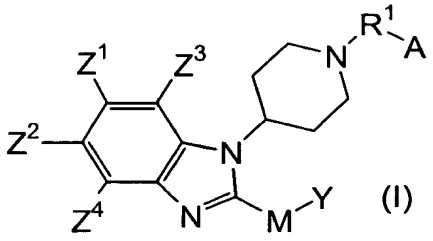
CLAIMS

1. A compound of the following formula:



(I)

or a salt thereof, wherein

R^1 is selected from the group consisting of $(C_3$-$C_{11})$cycloalkyl, $(C_6$-$C_{16})$bicycloalkyl, $(C_6$-$C_{16})$tricycloalkyl and $(C_8$-$C_{16})$tetracycloalkyl, wherein said groups are partially saturated, fully saturated or fully unsaturated and are optionally substituted with 1 to 3 substituents independently selected from the group consisting of halo, hydroxy, $(C_1$-$C_5)$alkyl and $(C_3$-$C_7)$cycloalkyl;

A is attached to the same carbon atom of R^1 that is also attached to the nitrogen atom of the piperidine ring, and is selected from the group consisting of $(C_1$-$C_7)$alkyl optionally substituted with 1 to 3 halo; $(C_2$-$C_5)$alkenyl; $(C_2$-$C_5)$alkynyl; phenyl-$(C_1$-$C_5)$alkyl optionally substituted at the phenyl moiety with 1 to 3 substituents; hydroxy-$(C_1$-$C_4)$alkyl; $(C_1$-$C_4)$alkoxy-(C=O); aryl optionally substituted with 1 to 3 substituents; and an aromatic or non-aromatic heterocyclic ring comprising four to ten ring atoms wherein one to four ring atoms are independently selected from nitrogen, oxygen and sulfur and said aromatic or non-aromatic heterocyclic ring is optionally substituted with 1 to 3 substituents, and the substituents attached to said phenyl moiety in the phenyl-$(C_1$-$C_5)$alkyl, aryl or heterocyclic ring is independently selected from the group consisting of halo; hydroxy; $(C_1$-$C_4)$alkyl optionally substituted with 1 to 3 halo; $(C_1$-$C_4)$alkoxy optionally substituted with 1 to 3 halo; $(C_1$-$C_4)$alkyl-CO-; phenyl; benzyl; -CHO; cyano; $(C_1$-$C_4)$alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; $(C_1$-$C_4)$alkyl-NH-; di[$(C_1$-$C_4)$alkyl]-N-; $(C_1$-$C_4)$alkyl-CO-NH-; $(C_1$-$C_4)$alkyl-NH-CO-; hydrazino; azido; ureido; amidino; guanidino; oxo and =N-OH;

M is selected from the group consisting of a single covalent bond, CH_2, O, S, SO, SO_2,

CO, NH, N[(C_1-C_6)alkyl], CONH and NHCO;

Y is selected from the following:

(e) 4- to 12-membered bicyclic-carbocyclic rings wherein said bicyclic-carbocyclic rings are optionally substituted with 1 to 6 substituents independently selected from the group consisting of halo, hydroxy, (C_1-C_4)alkyl optionally substituted with 1 to 3 halo; (C_1-C_4)alkoxy optionally substituted with 1 to 3 halo; (C_1-C_4)alkyl-CO-; phenyl; benzyl; -CHO; cyano; (C_1-C_4)alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; (C_1-C_4)alkyl-NH-; di[(C_1-C_4)alkyl]-N-; (C_1-C_4)alkyl-CO-NH-; (C_1-C_4)alkyl-NH-CO-; hydrazino; azido; ureido; amidino; guanidino; oxo and =N-OH, wherein the optionally substituted (C_1-C_4)alkyl are attached to the carbon or nitrogen atoms and other substituents are attached to the carbon atoms in the bicyclic-heterocyclic ring; with the proviso that said bicyclic-carbocyclic ring is not a benzofused ring;

(f) 4- to 12-membered bicyclic-heterocyclic rings wherein 1 to 6 ring atoms are independently selected from nitrogen, oxygen and sulfur wherein said bicyclic-heterocyclic rings are optionally substituted with 1 to 6 substituents independently selected from the group consisting of halo; hydroxy; (C_1-C_4)alkyl optionally substituted with 1 to 3 substituents independently selected from halo, hydroxy, (C_1-C_3)alkyl-SO_2NH_2- and $NH_2C(=O)NH$-; (C_1-C_4)alkoxy optionally substituted with 1 to 3 halo; (C_1-C_4)alkyl-CO-; aryl optionally substituted with 1 to 3 substituents independently selected from halo, (C_1-C_4)alkyl optionally substituted with 1 to 3 halo and (C_1-C_4)alkoxy; benzyl optionally substituted with 1 to 3 substituents independently selected from halo, (C_1-C_4)alkyl optionally substituted with 1 to 3 halo and (C_1-C_4)alkoxy; -CHO; cyano; (C_1-C_4)alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; (C_1-C_4)alkyl-NH-; di[(C_1-C_4)alkyl]-N-; (C_1-C_4)alkyl-CO-NH-; (C_1-C_4)alkyl-NH-CO-; hydrazino; azido; ureido; amidino; guanidino; oxo and =N-OH, wherein the optionally substituted (C_1-C_4)alkyl are attached to the carbon or nitrogen atoms and other substituents are attached to the carbon atoms in the bicyclic-heterocyclic ring; with the proviso that said bicyclic-heterocyclic ring is not a benzofused ring;

(g) 5- to 17 membered spirocarbocyclic rings wherein said spirocarbocyclic rings are optionally substituted with 1 to 6 substituents independently selected from the group consisting of halo; hydroxy; (C_1-C_4)alkyl optionally substituted with 1 to 3 halo; (C_1-C_4)alkoxy optionally substituted with 1 to 3 halo; (C_1-C_4)alkyl-CO-; phenyl; benzyl; -CHO; cyano; (C_1-C_4)alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; (C_1-C_4)alkyl-NH-; di[(C_1-C_4)alkyl]-N-; (C_1-C_4)alkyl-CO-NH-; (C_1-C_4)alkyl-NH-CO-; hydrazino; azido; ureido; amidino; guanidino; oxo and =N-OH;

(h) 5- to 17-membered spiroheterocyclic rings wherein 1 to 6 ring atoms are independently selected from nitrogen, oxygen and sulfur, wherein said spiroheterocyclic rings are optionally substituted with 1 to 6 substituents independently selected from the group consisting of halo; hydroxy; (C_1-C_4)alkyl optionally substituted with 1 to 3 halo; (C_1-C_4)alkoxy optionally substituted with 1 to 3 halo; (C_1-C_4)alkyl-CO-; phenyl; benzyl; -CHO; cyano; (C_1-C_4)alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; (C_1-C_4)alkyl-NH-; di[(C_1-C_4)alkyl])-N-; (C_1-C_4)alkyl-CO-NH-; (C_1-C_4)alkyl-NH-CO-; hydrazino; azido; ureido; amidino; guanidino; oxo and =N-OH; and

Z^1, Z^2, Z^3 and Z^4 are independently selected from the group consisting of hydrogen, halo, (C_1-C_4)alkyl optionally substituted with 1 to 3 halo; (C_1-C_4)alkoxy optionally substituted with 1 to 3 halo; (C_1-C_4)alkylsulfonyl; (C_1-C_4)alkyl-CO-; carboxy; (C_1-C_4)alkyl-COO-; amino; NH_2CO-; (C_1-C_4)alkyl-CO-NH-; (C_1-C_4)alkyl-SO_2-NH-; phenyl and naphthyl.

2. A compound according to Claim 1 or a salt thereof, wherein

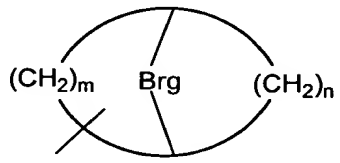
R^1 is (C_3-C_{11})cycloalkyl, wherein said cycloalkyl is partially saturated, fully saturated or fully unsaturated and is optionally substituted with 1 to 3 substituents independently selected from the group consisting of halo, hydroxy, (C_1-C_5)alkyl and (C_3-C_7)cycloalkyl;

A is attached to the same carbon atom of R^1 that is also attached to the nitrogen atom of the piperidine ring, and is selected from the group consisting of $(C_1$-$C_7)$alkyl optionally substituted with 1 to 3 halo; $(C_2$-$C_5)$alkenyl; $(C_2$-$C_5)$alkynyl; hydroxy-$(C_1$-$C_4)$alkyl; $(C_1$-$C_4)$alkoxy-(C=O); aryl optionally substituted with 1 to 3 substituents; and an aromatic or non-aromatic heterocyclic ring comprising four to six ring atoms wherein one to two ring atoms are independently selected from nitrogen, oxygen and sulfur and said aromatic or non-aromatic heterocyclic ring is optionally substituted with 1 to 3 substituents; and the substituents attached to said aryl or heterocyclic ring are independently selected from halo; $(C_1$-$C_4)$alkyl optionally substituted with 1 to 3 halo; $(C_1$-$C_4)$alkoxy optionally substituted with 1 to 3 halo; $(C_1$-$C_4)$alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; $(C_1$-$C_4)$alkyl-NH-; di[$(C_1$-$C_4)$alkyl]-N-; $(C_1$-$C_4)$alkyl-CO-NH- and $(C_1$-$C_4)$alkyl-NH-CO-;

M is selected from group consisting of a covalent bond, CH_2, O, S, SO_2, CO, NH, N[$(C_1$-$C_6)$alkyl), CONH and NHCO;

Y is selected from the following:

(a) bicyclic rings represented by formula Y1:

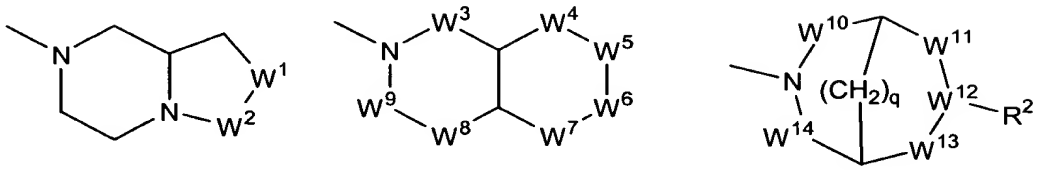


Y1

wherein m and n are independently 1, 2, 3 or 4; Brg is selected from $(CH_2)_p$ wherein p is 0, 1 or 2, and N-$(C_1$-$C_4)$alkyl; and Y1 is optionally substituted with 1 to 4 substituents independently selected from the group consisting of hydroxy; $(C_1$-$C_4)$alkyl optionally substituted with 1 to 3 halo; $(C_1$-$C_4)$alkoxy optionally substituted with 1 to 3 halo; $(C_1$-$C_4)$alkyl-CO-; phenyl; benzyl; $(C_1$-$C_4)$alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; $(C_1$-$C_4)$alkyl-NH-; di[$(C_1$-$C_4)$alkyl]-N-; $(C_1$-$C_4)$alkyl-CO-NH-; $(C_1$-$C_4)$alkyl-NH-CO-; oxo and =N-OH;

(b) 6- to 10-membered bicyclic-heterocyclic rings, containing 1 to 4 hetero atoms in

the ring, represented by formula Y2, Y3 or Y4:



Y2 Y3 Y4

wherein

W^1 is selected from CH_2, CH_2CH_2, O, S and NH;

W^2 is selected from CH_2, O, S, NH and C=O;

W^3 is selected from a covalent bond, CH_2, O, S, NH and C(=O)-NH;

W^4 is selected from a covalent bond, CH_2, O, S and NH;

W^5 is selected from a covalent bond, CH_2, $CH(CH_2OH)$, $CH(CH_2NHSO_2CH_3)$, $CH(CH_2NHC(=O)NH_2)$, CH_2CH_2, O, S, NH and C(=O);

W^6 is selected from CH_2, O, S, NH and $N[(C_1\text{-}C_4)alkyl]$;

W^7 is selected from a covalent bond, CH_2, O, S, NH and C(=O);

W^8 is selected from a covalent bond, CH_2, O, S and NH;

W^9 is selected from a covalent bond, CH_2, O, S, NH CH_2CH_2 and C(=O);

W^{10}, W^{11}, W^{13} and W^{14} are independently selected from covalent bond, CH_2, O, S, and NH;

W^{12} is selected from CH and N;

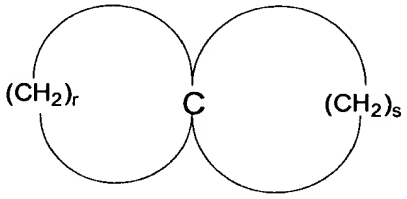
q is 1 or 2; and

R^2 is selected from hydrogen, $(C_1\text{-}C_4)alkyl$ and amino; and

said bicyclic-heterocyclic rings of formula Y2, Y3 or Y4 is optionally substituted with 1 to 4 substituents independently selected from the group consisting of halo; hydroxy; $(C_1\text{-}C_4)alkyl$ optionally substituted with 1 to 3 halo; $(C_1\text{-}C_4)alkoxy$ optionally substituted with 1 to 3 halo; $(C_1\text{-}C_4)alkyl\text{-}CO\text{-}$; ayrl optionally substituted with 1 to 3 substituents independently selected from halo, $(C_1\text{-}C_4)alkyl$ optionally substituted with 1 to 3 halo and $(C_1\text{-}C_4)alkoxy$; benzyl optionally substituted with 1 to 3 substituents independently selected from halo, $(C_1\text{-}C_4)alkyl$ optionally substituted with 1 to 3 halo and $(C_1\text{-}C_4)alkoxy$; -CHO; cyano; $(C_1\text{-}C_4)alkyl\text{-}CO\text{-}$; $NH_2\text{-}CO\text{-}$; $NH_2\text{-}CH_2\text{-}$; amino; $(C_1\text{-}C_4)alkyl\text{-}NH\text{-}$; $di[(C_1\text{-}C_4)alkyl]\text{-}N\text{-}$; $(C_1\text{-}C_4)alkyl\text{-}$

CO-NH-; (C_1-C_4)alkyl-NH-CO-; oxo and =N-OH;

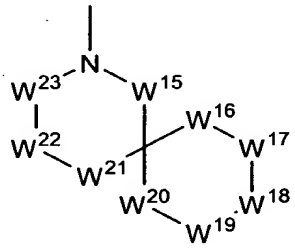
(d) spirocarbocyclic rings represented by formula Y5:



Y5

wherein r and s are independently 2, 3, 4 or 5; and said spirocarbocyclic ring or formula Y5 is optionally substituted with 1 to 4 substituents independently selected from the group consisting of hydroxy; (C_1-C_4)alkyl optionally substituted with 1 to 3 halo; (C_1-C_4)alkoxy optionally substituted with 1 to 3 halo; (C_1-C_4)alkyl-CO-; phenyl; benzyl; (C_1-C_4)alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; (C_1-C_4)alkyl-NH-; di[(C_1-C_4)alkyl]-N-; (C_1-C_4)alkyl-CO-NH-; (C_1-C_4)alkyl-NH-CO-; oxo and =N-OH; and either of monocyclic carbocyclic ring in Y5 is optionally fused to a benzene or (C_4-C_6)carbocyclic ring;

(d) 10- to 15-membered spiroheterocyclic rings, containing 1 to 4 hetero atoms in the ring, represented by formula Y6:



Y6

wherein

W^{15}, W^{16}, W^{17}, W^{18}, W^{19}, W^{20} and W^{23} are independently selected from the group consisting of a covalent bond CH_2, O, S and NH;

W^{21} is selected from the group consisting of a covalent bond CH_2, O, S, NH and N[(C_1-C_4)alkyl];

W^{22} is selected from the group consisting of a covalent bond CH_2, O, S, NH

and C(=O);

said spiroheterocyclic ring of formula Y6 is optionally substituted with 1 to 4 substituents independently selected from the group consisting of halo; hydroxy; (C_1-C_4)alkyl optionally substituted with 1 to 3 halo; (C_1-C_4)alkoxy optionally substituted with 1 to 3 halo; (C_1-C_4)alkyl-CO-; phenyl; benzyl; -CHO; cyano; (C_1-C_4)alkyl-CO-; NH_2-CO-; NH_2-CH_2-; amino; (C_1-C_4)alkyl-NH-; di[(C_1-C_4)alkyl]-N-; (C_1-C_4)alkyl-CO-NH-; (C_1-C_4)alkyl-NH-CO-; hydrazino; azido; ureido; amidino; guanidino; oxo and =N-OH; and optionally fused to a cyclohexane, benzene or pyridine ring; and

Z^1, Z^2, Z^3 and Z^4 are independently selected from the group consisting of hydrogen and halo.

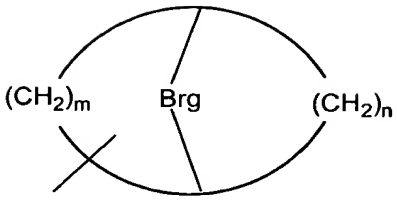
3. A compound according to Claim 2 or a salt thereof, wherein

R^1 is selected from the group consisting of (C_3-C_{11})cycloalkyl;

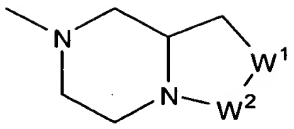
A is attached to the carbon atom of R^1, which is attached to the nitrogen atom of the piperidine ring, and selected from the group consisting of (C_1-C_7)alkyl, hydroxy-(C_1-C_2)alkyl, (C_1-C_4)alkoxy-(C=O), (C_2-C_5)alkenyl, phenyl and naphthyl;

M is selected from the group consisting of a covalent bond, CH_2, O, SO_2, CO, NH, N[(C_1-C_6)alkyl], and NHCO;

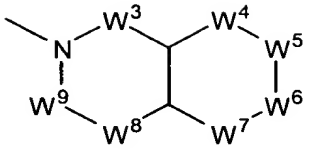
Y is selected from bicyclic rings represented by formula Y1; 6- to 10-membered bicyclic-heterocyclic rings, containing 1 to 4 hetero atoms in the ring, represented by formula Y2, Y3 and Y4; and 10- to 15-membered spiroheterocyclic rings, containing 1 to 4 hetero atoms in the ring, represented by formula Y6:



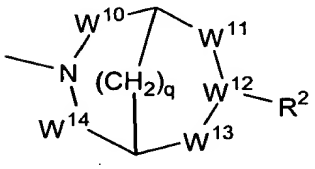
Y1



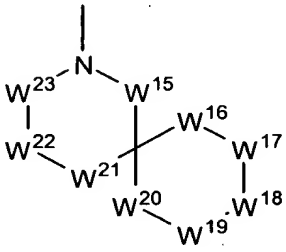
Y2



Y3



Y4



Y6

wherein

m and n are independently 1, 2, 3 or 4;

Brg is N-(C_1-C_4)alkyl;

W^1 is selected from CH_2, CH_2CH_2, O and NH;

W^2 is selected from CH_2 and C=O;

W^3 is selected from a covalent bond, CH_2 and C(=O)-NH;

W^4 is selected from a covalent bond, CH_2 and O;

W^5 is selected from a covalent bond, CH_2, $CH(CH_2OH)$, $CH(CH_2NHSO_2CH_3)$, $CH(CH_2NHC(=O)NH_2)$, CH_2CH_2 and C(=O);

W^6 is selected from CH_2, NH and N[(C_1-C_4)alkyl];

W^7 is selected from a covalent bond, CH_2 and C(=O);

W^8 is selected from a covalent bond and CH_2;

W^9 is selected from a covalent bond, CH_2, CH_2CH_2 and C(=O);

W^{10}, W^{11}, W^{13} and W^{14} are independently selected from a covalent bond and CH_2;

W^{12} is selected from CH and N;

q is 1 or 2; ;

R^2 is selected from hydrogen, (C_1-C_4)alkyl and amino;

W^{15}, W^{16}, W^{17}, W^{18}, W^{19}, W^{20} and W^{23} are independently selected from the group consisting of a covalent bond and CH_2;

W^{21} is selected from the group consisting of a covalent bond CH_2, NH and N[(C_1-C_4)alkyl];

W^{22} is selected from the group consisting of a covalent bond CH_2 and C(=O);

said group of formula of Y2, Y3 or Y4 is optionally substituted with 1 to 4 substituent independently selected from the group consisting of (C_1-C_4)alkyl; aryl optionally substituted with 1 to 3 substituents independently selected from halo, (C_1-C_4)alkyl optionally substituted with 1 to 3 halo and (C_1-C_4)alkoxy; and benzyl optionally substituted with 1 to 3 substituents independently selected from halo, (C_1-C_4)alkyl optionally substituted with 1 to 3 halo and (C_1-C_4)alkoxy; and

said group of formula Y6 is optionally fused to a cyclohexane, benzene or pyridine ring; and optionally substituted with 1 to 4 substituents independently selected from the group consisting of (C_1-C_4)alkyl, (C_1-C_4)alkoxy and aryl;

Z^1 and Z^2 are independently selected from the group consisting of hydrogen and halo; and Z^3 and Z^4 are both hydrogen.

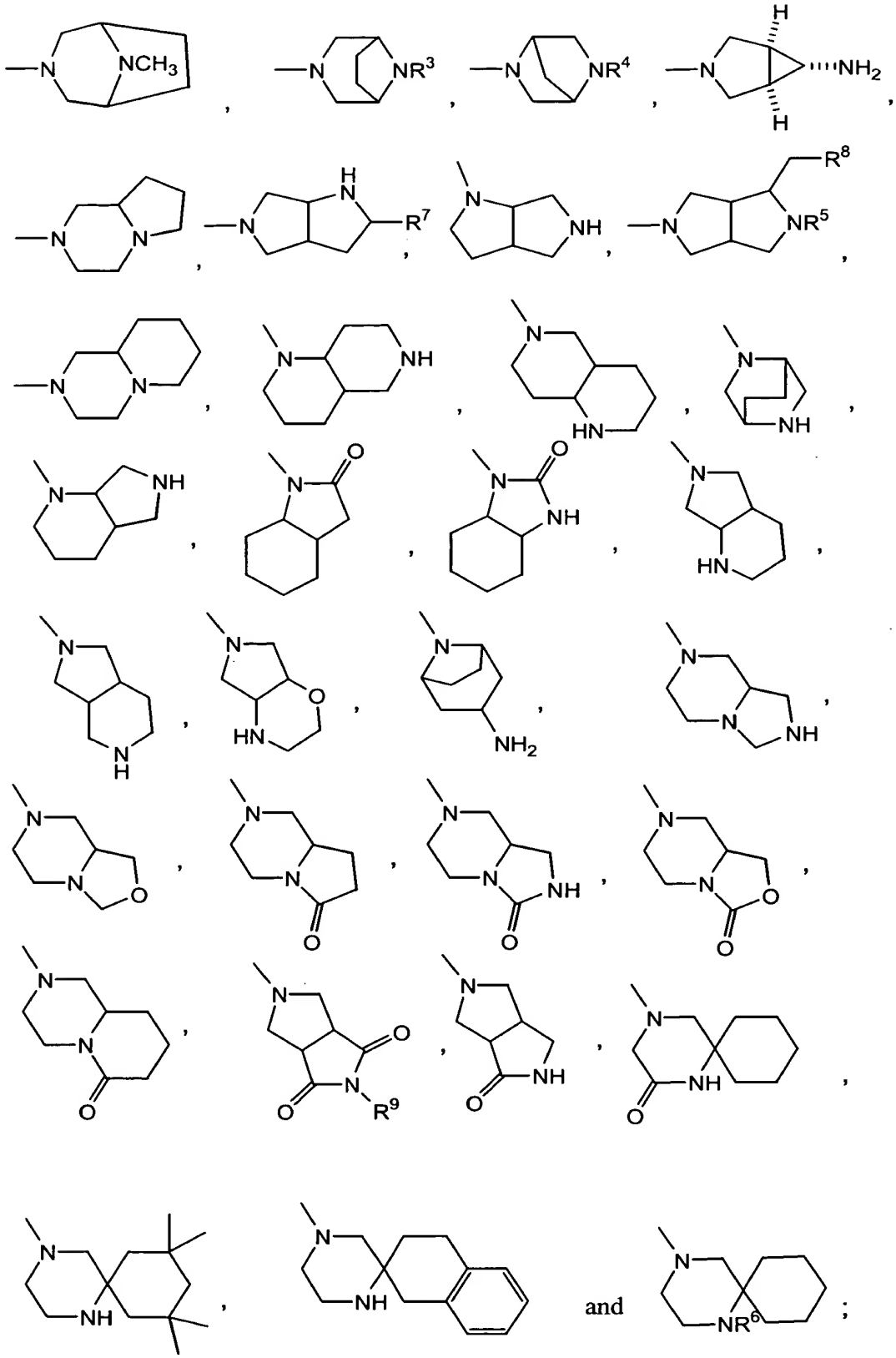
4. A compound according to Claim 3 or a salt thereof, wherein

R^1 is (C_6-C_{10})cycloalkyl;

A is attached to the carbon atom of R^1, which is attached to the nitrogen atom of the piperidine ring, and is selected from the group consisting of (C_1-C_7)alkyl and, phenyl l;

M is selected from group consisting of a covalent bond, CH_2, O, SO_2, CO, NH, N[(C_1-C_6)alkyl] and NHCO,

Y is selected from:



and

;

wherein R^3, R^4, R^5, R^6, R^7 and R^9 are independently selected from the group consisting of hydrogen and $(C_1$-$C_4)$alkyl;

R^8 is selected from the group consisting of hydroxy, $NHSO_2CH_3$ and $NHC(=O)NH_2$; and

Z^1, Z^2, Z^3 and Z^4 are all hydrogen.

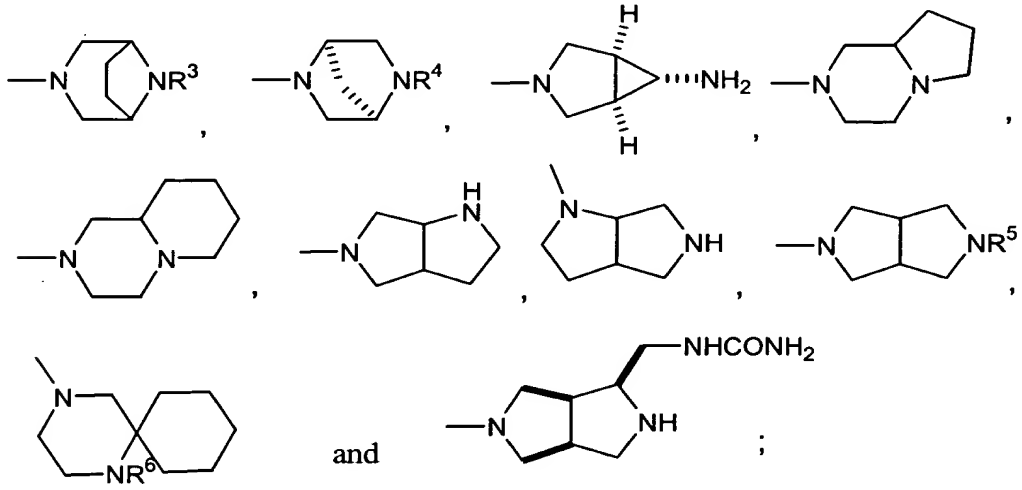
5. A compound according to Claim 4 or a salt thereof, wherein

R^1 is $(C_7$-$C_9)$cycloalkyl;

A is attached to the carbon atom of R^1, which is attached to the nitrogen atom of the piperidine ring, and is selected from the group consisting of methyl and phenyl;

M is selected from group consisting of a covalent bond, CH_2, O, CO, NH, $N[(C_1$-$C_6)$alkyl] and NHCO,

Y is selected from



;

wherein R^3, R^4, R^5 and R^6 are independently selected from the group consisting of hydrogen and $(C_1$-$C_4)$alkyl; and

Z^1, Z^2, Z^3 and Z^4 are all hydrogen.

6. A compound according to Claim 1 selected from

4-{1-[1-(1-methylcyclooctyl)-4-piperidinyl]-1*H*-benzimidazole-2-yl}-1,4-diazaspiro[5.5]undecane;

2-hexahydropyrrolo[3,4-c]pyrrol-2(1*H*)-yl-1-[1-(1-methylcyclooctyl)-4-piperidinyl]-1*H*-benzimidazole;

2-(3,8-Diazabicyclo[3.2.1]oct-3-yl)-[1-(1-methylcyclooctyl)-4-piperidinyl]-1*H*-benzimidazole; and

N-[(1SR, 3aRS, 6aSR)-5-{1-[1-(1-Methylcyclooctyl)-4-piperidinyl]-1*H*-benzimidazol-2-yl}octahydropyrrolo[3,4-*c*]pyrrole-1-ylmethl]urea; and a salt thereof.

7. A pharmaceutical composition for the treatment of a disorder or condition mediated by ORL1-receptor and its endogenous ligands in a mammal including a human, or for anesthetizing a mammal including a human, which comprises an effective amount of the compound of Claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

8. A pharmaceutical composition for the treatment of a disorder or condition selected from the group consisting of neuropathic pain, inflammatory diseases, inflammation-related hyperalgesia, eating disorders, arterial blood pressure disorders, tolerance to narcotic analgesics, dependence on narcotic analgesics, anxiety, stress disorders, psychic trauma, schizophrenia, Parkinson's disease, chorea, depressant, Alzheimer's disease, dementias, epilepsy and convulsions, useful as analgesics, anesthetics, neuroprotective agents or analgesic enhancers, or useful for controlling water balance, hearing regulation, controlling sodium ion excretion or ameliorating brain function, comprising an amount of a compound of Claim 1, or a pharmaceutically acceptable salt thereof that is effective in treating such disorder or condition in a mammal including a human, and a pharmaceutically acceptable carrier.

9. A method of treating a disorder or condition, or anesthetizing a mammal including a human, the treatment and anesthetization of which can be effected or facilitated by activating ORL1-receptor in a mammal including a human, comprising administering to a mammal in need of such treatment an effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt thereof.

Sub B1

10. A method for treating a disorder or condition in a mammal including a human, where the disorder or condition is selected from the group consisting of neuropathic pain, 1inflammatory diseases, inflammation-related hyperalgesia, eating disorder, arterial blood pressure disorders, tolerance to narcotic analgesics, dependence on narcotic analgesics, anxiety, stress disorders, psychic trauma, schizophrenia, Parkinson's disease, chorea, depressant, Alzheimer's disease, dementias, epilepsy and convulsions, or for anesthetizing a mammal including a human, or for alleviating pain, producing a neuroprotective effect, enhancing analgesic, controlling water balance, hearing regulation, controlling sodium ion excretion or ameliorating brain function in a mammal including a human, comprising administering to said mammal an effective amount of a compound of Claim 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

add B2